UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,375	10/30/1998	JANOS SZEBENI	003/098/SAP	3056

7590 07/11/2006

Venable
1201 New York Avenue N.W.
Suite 1000
Washington, DC 20005-3917

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/183,375	SZEBENI ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-11,16-19,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *7-9,11,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 10, 16, 17, 21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 4-21-06 is acknowledged.

Claims included in the prosecution are 1-4, 10, 16, 17, 21 and 22.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 10, 16, 17, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of complementation activation by sCR1, does not reasonably provide enablement for several inhibitors recited in the independent claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. It is well known that complement system is a complicated system and the activation of the complement can occur via at least two pathways: one involves antigen-antibody complexes. Applicant recites EGTA as one of the inhibitors. According to US 6,495,735, EGTA is a chelator, which removes calcium, which is essential for classical pathway complement activation, and so the presence of EGTA ensures that complement can only be activated by the alternative pathway (col. 14, lines 4-10). Applicant has not shown that all the inhibitors recited in the claims are able to inhibit the complement activation system, which is activated by cremophor. For example, at least one of the inhibitors recited in the claims, zymosan is not an inhibitor at all and is recognized in the

art as an activator (Ravetch et al, 5,877,396; col. 52, lines 25-30). Because the system is complex, one cannot predict based on the results obtained by one inhibitor that other inhibitors would also have the same effect. This is evident from the above-cited references. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to the inhibitor, sCR1 which is shown to be effective against the side effects of cremophor.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-4, 10, 16, 17, 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what GS1, PAP, ClqInh, compound K-76COOH, small peptide analogs of the C terminal part of C3, CAB-2 represent as recited in the independent claims. 'small' is a relative term and therefore, is indefinite. The meets and bounds of diamines, small polyanions, sulfonated aromatic compounds are unclear. 'Indomethacin' is misspelled in the independent claims.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-4, 10, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Lodge (5,462,726).

Lodge discloses a method of inhibiting the side effects of solvents containing Cremophor (polyethoxylated castor oil) and/or drugs such as taxol or cyclosporine. The compositions contain cremophor, Taxol or cyclosporine and thromboxane A2 receptor antagonist, indomethacin. The compositions further contain ethanol. Indomethacin is administered together or prior to or after the administration of the composition. The toxic side effects referred to by Lodge are deemed to include toxicity expressed as hypersensitivy (abstract, col. 1, lines 27-61, col. 2, lines 20 through col. 3, line 7, col. 5, line 52 through col. 7, line 10, Example 20).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-4, 6, 10, 16-17 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terwogt (cancer Treatment Reviews, March 1997) or O'Brien (Annals of Oncology, 1992) in view of Ko (5,851,528) and applicant's statements of prior art.

Terwogt teaches that that the antitumor drug paclitaxel is usually administered in combination with the vehicle, cremophor EL (polyethoxylated castor oil) and the administration of this combination causes severe hypersensitivity reactions (pages 88-89). What is lacking in Terwogt is the teaching of the administration of compliment activation inhibitors.

O'Brien teaches that several cytotoxic drugs including Taxol and doxorubicin cause hypersensitivity reactions (abstract and Table 2).

Ko teaches that compliment system includes a group of proteins in blood plasma, which plays an integral role in immune and allergic reaction and discloses a method of inhibiting complement activation by administering complement activation inhibitors. The method involves the administration of the inhibitor in controlled release delivery devices such as liposomes. The method is used for various conditions including the drug induced allergies and inflammation (note the abstract, col. 3, lines 49-52, col. 5, lines 32-51, col. 11, lines 1-42, examples and claims). Ko is also suggestive of the administration of the inhibitor along with the drug from his statements on col. 10, line 42 et seq., according to which the inhibitor "can be combined with appropriate pharmaceutical formulation. Ko however, does not specifically teach instant drugs or

carriers such as Cremophors. Ko does not teach claimed complement activator inhibitors.

Applicant on page 22 indicates that the claimed inhibitors are known in the art.

In essence the reference of Terwogt shows the problems (hypersensitivity) associated with the commonly used drug-carrier (paclitaxel-Cremophor) combination and that of O'Brien shows that several drugs cause allergic (hypersensitivity) reactions. The reference of Ko offers a solution and applicant's statements of prior art indicate that the claimed inhibitors are art known.

To use complement activation inhibitors to reduce or inhibit the hypersensitivity reactions caused by paclitaxel-cremophor EL combination or that caused by drugs such as doxorubicin and others would have been obvious to one of ordinary skill in the art since Ko teaches that administration of complement activation inhibitor would reduce the allergies and inflammation caused by the drugs. To use art known inhibitors with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since Ko teaches that a group of proteins play a role in the activation of the complement system which includes immune and allergic reactions and is suggestive of that one such inhibitor is effective in alleviating various conditions. The criticality of the administration of the compliment activation inhibitor prior to the administration of the drug is unclear to the examiner since it would be obvious to one of ordinary skill in the art that such an administration would prevent the active agent or the carrier from activation of the compliment system. The criticality of the active agent in claim 17 is also unclear to the examiner since the claims are drawn to the inhibition of the

hypersensitivity reactions by the compliment activation inhibitor and hemoglobin is known to be administered to anemic patients. Compliment inhibition by the inhibitor occurs irrespective of the nature of the drug.

9. Claims 1-4, 6, 10 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terwogt (cancer Treatment Reviews, March 1997) or Lodge cited above, further in view of Wheeler (5,478,860).

Terwogt as pointed out above, teaches that that the antitumor drug paclitaxel is usually administered in combination with the vehicle, cremophor EL (polyethoxylated castor oil) and the administration of this combination causes severe hypersensitivity reactions (pages 88-89). What is lacking in Terwogt is the teaching of the administration of compliment activation inhibitors such as indomethacin.

The teachings of Lodge have been discussed above. Lodge does not explicitly teach that the toxic side effects as hypersensitivity.

Wheeler teaches that Cremophor can promote acute toxic reactions typically expressed as hypersensitivity and it is managed clinically by the use of with anti-inflammatory agents (col. 1, lines 30-39).

The use of anti-inflammatory agents such as indomethacin in the teachings of Terwogt would have been obvious to one of ordinary skill in the art since Wheeler teaches that the treatment of the hypersensitivy reactions caused by Cremophor are known to be treated with anti-inflammatory agents. Although Lodge does not explicitly teach that the toxic side-effects include hypersensitivity reaction, such would have been

obvious to one of ordinary skill in the art since Wheeler teaches that acute toxic reactions are typically expressed as hypersensitivity reaction.

10. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lodge cited above.

Lodge as pointed out above, discloses a method of inhibiting the side effects of solvents containing cremophor (polyethoxylated castor oil) and drugs such as taxol or cyclosporine. The compositions contain cremophor, Taxol or cyclosporine and indomethacin. The compositions further contain ethanol. Indomethacin is administered together or prior to or after the administration of the composition (abstract, col. 2, lines 20 through col. 3, line 7, col. 5, line 52 through col. 7, line 10, Example 20). Lodge lacks the teachings of claimed drugs such as doxorubicin (instant claim 16) or polynucleotides of hemoglobin (claim 17). However, since Lodge further teaches that the thromboxane receptor antagonist can be used even for the side effects caused by the drug itself (abstract), it would have been obvious to one of ordinary skill in the art to use the compositions of Lodge if drugs such as doxorubicin and polynucleotides have the unwanted side effect with a reasonable expectation of success based on the guidance provided by Lodge.

Applicant's arguments have been fully considered, but are deemed to be moot in view of the new rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is

(571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK